

Attorney Docket No.: KUZ0028US.NP
Inventors: Tateishi et al.
Serial No.: 10/566,350
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REMARKS

Claims 1, 3-9, 11 and 13-20 were pending in the instant application. Claims 1, 3-9, 11 and 13-20 have been rejected. Claims 1, 8 and 9 have been amended. Claims 3, 4, 7 and 13-19 have been canceled. New claims 21-31 have been added. Support for these amendments is provided in the original claims and throughout the specification, for example, in Table 1 at page 28 and Figure 2, as well as paragraphs [0026] and [0039 through [0046]. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of the amendments and the following remarks.

Rejection of Claims under 35 U.S.C. 103(a)

The Examiner has maintained the rejection of claims 1, 3-9, 11 and 13-20 under 35 U.S.C. 103(a) as being unpatentable over Modamio et al. (Int. J. Pharmaceutics 1998 173:141-148) in view of Hirano et al. (U.S. Patent 6,495,159) and Higo et al. (U.S. Patent 5,866,157) as further evidenced by Walters (Transdermal Drug Delivery, 1989, New York, NY, pp 97-246).

Applicants respectfully traverse this rejection.

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Claim 1 has been amended to be drawn to an adhesive patch having a pressure-sensitive adhesive layer comprising bisoprolol and/or a pharmaceutically acceptable salt thereof, wherein said adhesive layer is a matrix type, and the composition thereof contains 2-ethylhexyl acrylate·vinyl acetate·acrylic acid copolymer, a percutaneous absorption promoter selected from the group consisting of lauryl alcohol, myristyl alcohol, oleyl alcohol, isostearyl alcohol, diethyl sebacate, lauric acid diethanolamide, isopropyl myristate, glycerol monocaprate, glycerol monolaurate, glycerol monooleate, sorbitan monolaurate, propylene glycol monolaurate, polyoxyethylene lauryl ether, and pyrothiodecane, and an organic acid and/or a pharmaceutically acceptable salt thereof, and the penetration rate of bisoprolol through skin is 4-300 $\mu\text{g}/\text{h}\cdot\text{cm}^2$. Support for these amendments is provided in claims 4, 7 and 16, now canceled.

Further, Applicants have added new dependent claims 21 through 31 drawn to compositions of the present invention as set forth in Examples 3 through 8 of the instant specification.

None of the cited references teach use of 2-ethylhexyl acrylate·vinyl acetate·acrylic acid copolymer as claimed.

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Nor do any of the cited references teach or suggest use of this copolymer in combination with bisoprolol as claimed. Further, none of the cited references teach or suggest a combination of more than two percutaneous absorption promoters, and in particular, a combination of a percutaneous promoter and an organic acid and/or a pharmaceutically acceptable salt thereof, as claimed.

Accordingly, the cited combination of references does not teach or suggest all elements of the claimed invention and therefore cannot render obvious the instant claimed invention.

Further, as evidenced by Examples 3 through 8 of the instant specification, compositions comprising both an absorption promoter and an organic acid as claimed exhibited a much higher percutaneous absorption rate of bisoprolol as compared to Examples 1 and 2 comprising either an absorption promoter or an organic acid. Specifically, the skin penetration rate of bisoprolol exhibited by compositions of Examples 3 through 8 of the instant specification was at least about $34.0 \mu\text{g}/\text{h}\cdot\text{cm}^2 \pm \text{S.E.}$ See Table 1 at page 28 of the instant specification as well as Figure 2. This absorption rate is significantly higher than the $1.9 \pm 0.6 \mu\text{g}/\text{h}\cdot\text{cm}^2$ penetration rate disclosed by Modamio as well as

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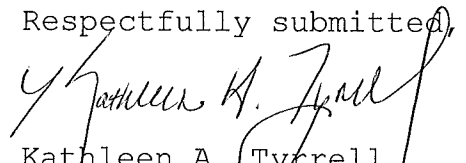
three standard deviations above. See page 6 of the Office Action mailed February 27, 2009. Achieving this significantly higher penetration rate with the instant claimed combination of elements was completely unexpected over teachings of the cited references and rebuts any prima facie obviousness over the combination of cited references. See MPEP 2141.

Withdrawal of this rejection is respectfully requested.

Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,


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